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& HEALTH

John Vandenberg, PhD
Director of Research at NCEA
109 T.W. Alexander Drive
Research Triangle Park, NC 27709

Sent via e-mail

RE: FOLLOW-UP TO THE MEETING AT RTP

Dear Dr. Vandenberg,

August 23, 2016

Ramboll Environ
28 Amity Street
Suite 2A
Amherst, MA 01002
USA

T +1 413 8354350
www.ramboll-environ.com

Thank you for setting up and orchestrating the "listening session" on Tuesday August 9th, 2016 at your offices. Dr. Gentry and I appreciate the opportunity to present the findings from our independent review of chloroprene's potential carcinogenicity, based on all available data and state-of-the-art methods for critically reviewing and synthesizing epidemiology, toxicology and mechanistic studies, and for integrating evidence across these lines of inquiry.

As discussed after our presentation of the science, we acknowledge and appreciate your explanation of the IRIS Program's resource constraints, the complex procedures in place for selecting substances for IRIS review or re-review, as well as what you described as the "full docket" of current and future IRIS reviews. Based on this feedback, we understand that the IRIS Program will not at this time undertake a new review of chloroprene – or consider any revisions to the risk numbers – primarily due to resource constraints.

This, as you can understand, leaves our client, Denka Performance Elastomer, LLC (DPE), in a very difficult position, and unjustifiably so from a scientific standpoint. During our meeting, we outlined important new information demonstrating that an IRIS chloroprene IUR derived today would be vastly different and more compatible with other IURs for other chemicals. As we demonstrated during our meeting, properly employing validated PBPK models leads to an IUR for chloroprene that is more than 100-fold lower than the 2010 IRIS value. In fact, the 2010 IRIS Review of Chloroprene astutely acknowledged this very flaw: "Ideally, a PBPK model for the internal dose(s) of the reactive metabolite(s) would decrease some of the quantitative uncertainty in interspecies extrapolation; however, current PBPK models are inadequate for this purpose" (US EPA, 2010, Section 3) [1]. The information and methods required for chloroprene now have been peer-reviewed, published, and validated, with similar models and methods applied by EPA in comparable risk evaluations (such as vinyl chloride).

[1] US EPA 2010. Toxicological Review of Chloroprene. In support of Summary Information on the Integrated Risk Information System. Washington, DC: U.S. Environmental Protection Agency.

We also noted what we consider a misinterpretation of the body of epidemiological evidence, largely due to discounting the negative results published from the 2007 Marsh et al. study, which is also the strongest epidemiological study, in favor of results from much weaker studies. The integration of the entirety of epidemiological evidence supports the updated toxicology and mechanistic evidence indicating important and substantial differences between humans and mice, specifically in terms of metabolism, which are directly related to estimating the potential cancer risks for chloroprene. This no longer can be ignored. Taking the most up-to-date information into consideration in the context of using science to inform EPA policy and regulation is entirely consistent with the Agency's very public "mission statement" to ensure that "national efforts to reduce environmental risk are based on the best available scientific information." [2]

Without a commitment on the Agency's part to reexamine the 2010 IRIS assessment's IUR derivation in light of the new information, EPA and the Louisiana Department of Environmental Quality have advised DPE that it will be required to meet extremely stringent emissions limits, which may not be attainable, and that are not based on the best available science. We also have seen that the IUR is being used to inform important regulatory and other federal and state government actions, as well as public statements with respect to the possible cancer risks to people who live and work in the community in which our client's facility is located.

Notwithstanding the IRIS Program's resource constraints, we genuinely look forward to any thoughts or ideas you or Dr. Cogliano might have with respect to how we might work collaboratively with you and the program office within EPA that is relying on the 2010 IRIS Assessment, to timely improve and update the IUR. The IUR for chloroprene (as well as actions that are derivative of that IUR) should be more in line with those of other substances, such as vinyl chloride, that provide stronger evidence than chloroprene of carcinogenicity in humans.

We, too, will be exploring various available avenues, and will keep you informed. One possibility would be for us to file a request for correction (RFC). Our ultimate goal, as I initially mentioned to Dr. Cogliano when I first approached him, is to improve the risk calculation based on currently available science and evidence-based processes, which have evolved since the completion of the 2010 Chloroprene Toxicological Review, and to do so in a way that creates the lowest demands on already limited resources. Thank you again, and I look forward to continuing our discussion.

Yours sincerely

Kenneth A. Mundt, PhD, FACE
Health Sciences Practice Network Leader
D +1 413 835 4360
M +1 413 885 1345
kmundt@ramboll.com

cc: Dr. Vincent Cogliano

[2] https://www.epa.gov/aboutepa/our-mission-and-what-we-do